

MMHCC Newsletter September 2005

MouseLine

"Jumping" DNA: A Tool for Finding Cancer Genes



Researchers have developed a new method of inducing cancer in mice and then rapidly identifying the genes involved. The mice are engineered to carry bits of DNA called transposons that, in the presence of a particular protein, jump randomly around the chromosomes of mouse cells, occasionally landing in genes and causing mutations.

As genetic mutations accumulate, the mice develop aggressive tumors and die. Researchers can pinpoint which genes were mutated by tracking molecular "tags" that mark where the transposons inserted themselves. Commonly mutated genes in mouse tumors may be versions of cancer genes in people. "We think this is a powerful way to identify cancer genes for many different cancers," says Dr. Neal Copeland of the Mouse Cancer Genetics Program in the National Cancer Institute's (NCI's) Center for Cancer Research. "A number of the cancer genes we have found so far in the mice are known cancer genes in humans." The researchers have also identified some potentially novel cancer genes. One of the new method's appealing features is that no prior knowledge about the genetics of a tumor is required to search for genes.

The project was started by Drs. David Largaespada and Adam Dupuy at the University of Minnesota in Minneapolis in 1997. A few years ago, Dr. Dupuy brought the transposon technology to NCI, where he has been working with Drs. Copeland and Nancy Jenkins. The Minnesota and NCI groups collaborated while testing the method in different types of mice. Regardless of genetic background, the mice all died within 120 days, and some developed multiple tumors, according to findings in the July 14 *Nature*.

Dr. Largaespada began the project just as colleagues at the University of Minnesota had created a modified transposon using a version from salmon. Like almost all DNA transposons in vertebrates, it had not functioned for millions of years, but the researchers eliminated genetic mutations that had rendered it immobile, causing an "awakening."

Named *Sleeping Beauty*, the transposon has been used to induce mutations in the sperm and eggs of mice. But the transposon was not active enough to cause tumors, so the challenge was to increase the frequency of movement from one chromosomal location to another. The researchers succeeded, and the new *Sleeping Beauty* transposon system can cause tumors in a variety of tissues throughout the lifetime of a mouse, providing another tool for finding cancer genes and potential leads for treatments.

"In some mice, clusters of gene mutations accumulate over time, and you begin to see a tumor's genetic 'fingerprint,'" says Dr. Largaespada. "This is important because the most effective cancer treatments may be combinations of drugs that attack each mutant gene product."

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Dr. Dupuy recently modified the system so that *Sleeping Beauty* can be made to jump in specific tissues rather than around the whole body. The researchers are developing mice that can be used to investigate breast, colon, and prostate cancer in people.

The mice could also help researchers sift through the avalanche of mutations routinely identified in human tumors. For example, the proposed cancer genome project, which is in a pilot project planning phase, will need tools for identifying mutations that actually contribute to the disease, as opposed to just being present in tumors.

Source: NCI Cancer Bulletin, July 26, 2005; Volume 2 / Number 30

Meetings

October 19-23, 2005

Colon Cancer

AACR Special Conference

Dana Point, California

Meeting information: <http://www.aacr.org/default.aspx?p=3625>

Abstract deadline: September 16, 2005

October 30- November 2, 2005

International Conference on Frontiers in Cancer Prevention Research

AACR Special Conference

Baltimore, MD

Meeting information: <http://www.aacr.org/default.aspx?p=4185>

Abstract deadline: September 15, 2005

For additional information about meetings and workshops, please go to:

<http://emice.nci.nih.gov/emice/communication/calendar>

Funding Opportunities

September SCAW Advanced IACUC Workshop in North Carolina

(NOT-OD-05-054)

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-054.html>

IACUC 101 Workshop in Rochester, New York, in October

(NOT-OD-05-066)

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-066.html>



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tarnowsb@mail.nih.gov Send meeting announcements and other information you would like to
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Funding Opportunities cont.

October SCAW Advanced IACUC Workshop in Chicago, Illinois

(NOT-OD-05-070)

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-070.html>

November 6 IACUC 101 Training to be held in St. Louis, Missouri

(NOT-OD-05-056)

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-056.html>

Notice of Intent to Publish Four Requests for Applications (RFAs) for Knockout Mouse Project (KOMP)

(NOT-OD-05-063)

National Institutes of Health

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-063.html>

Specialized Programs of Research Excellence (SPOREs) in Human Cancer for Year 2006

(PAR-05-156)

National Cancer Institute

Application Receipt Date(s):

Breast Cancer SPORE: February 1, 2006

Gastrointestinal (GI) Cancer, Brain Cancer, and Lymphoma SPOREs: June 1, 2006

Head & Neck Cancer and Prostate Cancer SPOREs: October 1, 2006

<http://grants.nih.gov/grants/guide/pa-files/PAR-05-156.html>

Addendum: <http://grants.nih.gov/grants/guide/notice-files/NOT-CA-05-027.html>

Animal Models of Diabetic Complications Consortium

(RFA-DK-05-011)

National Institute of Diabetes and Digestive and Kidney Diseases, National Heart, Lung, and Blood Institute, National Institute of Neurological Disorders and Stroke

<http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-05-011.html>



NCI's Mouse Repository News

The MMHCC Mouse Repository is an NCI-supported resource for the distribution of mouse cancer models and associated strains. The Repository makes strains available to all members of the scientific community; up to 3 breeder pairs of each available strain may be ordered.

Newly accepted strains:

The following strains have recently been accepted into the MMHCC Repository and are available or will be soon available for distribution (please click on the specific link, below, for additional information):

- 1) B6;129-*E2f4*^{tm1Lees} (E2f4)
http://mouse.ncicrf.gov/available_details.asp?ID=01XK7
- 2) B6;129S-*E2f3*^{tm1Lees} (E2f3)
<http://mouse.ncicrf.gov/details.asp?ID=01XK6>

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